

Claims

1. Protein mixture comprising:
 - a) at least a first fusion protein comprising:
 - i) a protein or protein fragment,
 - ii) an interaction domain and
 - iii) a protein translocation sequence which effects that the fusion protein upon expression in a bacterium is translocated through the cytoplasmic membrane in an essentially unfolded state,and
 - b) at least a second fusion protein comprising:
 - i) a protein or protein fragment,
 - ii) an interaction domain and
 - iii) a protein translocation sequence which effects that the fusion protein upon expression in a bacterium is translocated through the cytoplasmic membrane in an essentially folded state,wherein the interaction domain of the first fusion protein can bind to those of the second fusion protein.
2. Protein mixture according to claim 1, wherein the protein or protein fragment of the first fusion protein is an immune globulin heavy chain, an immune globulin light chain, a single chain antibody, a diabody, a receptor, a receptor ligand, an integrin, an intimin, a carbohydrate binding protein, an albumin binding protein or protein A.
3. Protein mixture according to claims 1 or 2, wherein the protein or protein fragment of the second fusion protein is an autofluorescent protein, in particular GFP or a variant thereof, an enzyme, a cofactor-dependent protein, a protein that is encoded by a cDNA derived from a cDNA library or a synthetic protein.
4. Protein mixture according to claim 1, wherein the protein or the protein fragment of the first fusion protein and the protein translocation sequence is a phage coat protein, a

periplasmatic marker enzyme, an intimin, a protein of the outer bacterial membrane or a periplasmatic receptor protein.

5. Protein mixture according to claim 4, wherein the phage coat protein is selected from the M13 phage coat proteins pIII, pVI, pVII, pVIII and pIX.
6. Protein mixture according to claims 1 to 5, wherein the interaction domains of the first and the second fusion protein are each respectively a leucine zipper domain and a leucine zipper domain, a helix-loop-helix-domain and a helix-loop-helix-domain, a calmodulin and a calmodulin binding peptide or a peptid dimer pair of naturally or synthetic origin.
7. Protein mixture according to one of claims 1 to 6, wherein the protein translocation sequence of the first fusion protein is a Sec-dependent, a SRP-dependent, a YidC-dependent sequence or a transport pathway-independent sequence which is integrated into the membrane.
8. Protein mixture according to one of claims 1 to 7, wherein the protein translocation sequence of the second fusion protein is a Tat dependent or Δ -ph dependent sequence.
9. Protein mixture according to one of claims 1 to 8, wherein the protein is covalently or non-covalently bound to the second fusion protein.
10. Nucleic acid mixture coding for a protein mixture according to one of claims 1 to 8.
11. Nucleic acid mixture according to claim 10, wherein at least two nucleic acids which code for different fusion proteins are covalently attached to each other.
12. Vector comprising a protein mixture according to one of claims 1 to 9 and/or a nucleic acid mixture according to one of claims 10 or 11.
13. Cell comprising a protein mixture according one of claims 1 to 9, a nucleic acid mixture according to one of claims 10 or 11 and/or a vector according to claim 12.

14. Library comprising at least two protein mixtures according to one of claims 1 to 9, at least two vectors according to claim 12 and/or at least two cells according to claim 13, wherein the proteins or protein fragments of the respective first or the respective second fusion protein are different from each other.
15. Method of identifying a substance, which can bind to a protein mixture according to one of claims 1 to 9, to a vector according to claim 12 or to a cell according to claim 13 comprising the steps:
 - a) contacting at least one potentially binding substance with a protein mixture according to one of claims 1 to 9, a vector according to claim 12, and/or a cell according to claim 13 and
 - b) determining of the binding of the potentially binding substance to the protein mixture, the vector and/or the cell.
16. Method of identifying proteins or protein fragments, which bind to a test substance comprising the following steps:
 - a) contacting at least one test substance with a library according to claim 14 and
 - b) measuring of the respective binding of the test substance to the different protein mixtures, vectors and/or cells of the library.
17. A method according to claim 16 comprising the further steps:
 - a) selecting at least one protein mixture, one vector or one cell on the basis of the measured binding and
 - b) generating a second library wherein the library is generated by modification of the protein or protein fragment comprised in the selected protein mixture, in the selected vector or in the selected cell.
18. Method according to claim 16 comprising the further steps:

- a) selecting at least one protein mixture, one vector or one cell on the basis of the measured binding,
 - b) producing a second library wherein the library is created through the modification of the proteins or protein fragments comprised in the selected protein mixture, in the selected vector or in the selected cell,
 - c) contacting at least one test substance with second library,
 - d) measuring of the respective binding of the test substance to the different protein mixtures, vectors or cells of the second library and
 - e) if the case may be repeating of steps a) to d) until a protein mixture, a vector or a cell is selected which exhibits the desired binding.
19. Method according to one of the claims 15 to 18, wherein in a further step the binding substance of the protein or protein fragment or a variant thereof comprised in the selected protein mixture, in the selected vector or in the selected cell is mixed with a pharmaceutical acceptable carrier and/or auxiliary substance.
20. Kit for the production of a nucleic acid mixture according to claim 10 comprising:
- a) at least a first nucleic acid comprising at least a first restriction site 5' and/or 3' of a nucleic acid coding for a first fusion protein comprising:
 - i) an interaction domain and
 - ii) a protein translocation sequence which effects that the first fusion protein upon expression in a bacterium is translocated through the cytoplasmic membrane upon expression in a bacterium in an essentially folded state.
21. Kit according to claim 20 further comprising:

- a) at least a second nucleic acid comprising at least one restriction site 5' and/or 3' of an nucleic acid coding for a second fusion protein comprising:
 - i) an interaction domain and
 - ii) a protein translocation sequence which effects that the second fusion protein upon expression in a bacterium is translocated through the cytoplasmic membrane in an essentially unfolded state,

wherein the interaction domain of the first fusion protein can bind to those of the second fusion protein.

- 22. Use of a cell according to claim 13 for the production of a protein mixture according to one of claims 1 to 9.
- 23. Use of a protein mixture according to one of claims 1 to 9, a vector according to claim 12 and/or a cell according to claim 13 for the production of the library according to claim 14.